Objection to the specification

The specification was objected to because the Brief Description of the Drawings section failed to describe each and every figure disclosed. As requested by the Examiner, the Applicants have amended the Brief Description of the Drawings to describe the drawings individually. Support for these amendments is found throughout the specification, and, in particular, at page 13, line 3 through page 15, line 6, in Example 3, starting on line 31 through page 22, line 5, and in Figures 2-7.

Specifically, support for the apparatus depicted in Figure 2 is found on page 20, line 33 to page 21, line 6. Support for the apparatus depicted in Figure 3 is found on page 21, lines 7-11. Support for the apparatus depicted in Figure 4 is found on page 21, lines 12-24. Support for the apparatus depicted in Figure 5 is found on page 21, lines 25-32. Figure 6 is another view of the apparatus of Figure 4. And support for the apparatus depicted in Figure 7 is found on page 21, line 33 to page 22, line 5.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected Claim 22 under 35 U.S.C. § 112, second paragraph because the Examiner asserts that the phrase "almost symmetrically" is vague and indefinite because it is not clear what angle(s) would encompass "almost symmetrically."

Although Applicants maintain that one of skill in the art can readily determine the meaning of the terminology "almost symmetrically," Applicants have amended Claim 22 to recite that the two illuminate sources are positioned to allow the detection of the precipitate(s). This amendment is supported throughout the specification and, in particular page 13, lines 18-22.

In view of the above, the Applicants respectfully request withdrawal of the rejection of Claim 22 under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 101

The Examiner rejected Claim 23 under 35 U.S.C. § 101 on the assertion that it was directed to non-statutory subject matter.

The Applicants have amended Claim 23 to recite a computer comprising program code stored thereon for determining the possible presence of a precipitate in discrete regions. As a

computer is clearly statutory subject matter, Applicants respectfully request withdrawal of the rejection of Claim 23 under 35 U.S.C. § 101.

Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 1-26 under 35 U.S.C. § 103(a) in view of Abouzied et al. (*Journal of AOAC International*, 1994, Vol. 77, No. 2, pp. 495-501) and view of Howard III et al (EP 0 646 784 A1) and in further view of Roth et al. (U.S. Patent No. 5,902,727), Terstappen et al. (U.S. Patent No. 5,646,001) and Brown (U.S. Patent No. 5,807,522).

In order for a combination of references to render a claim obvious, the combination of references must teach or suggest each of the elements of the claimed invention and must also provide the motivation to combine these elements to create the claimed invention. *In re Fine*, 5 U.S.P.Q.2d 1597 (Fed. Cir. 1988), *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1456 (Fed. Cir. 1998) and *In re Geiger*, 2 U.S.P.Q.2d 1276 (Fed. Cir. 1987). As discussed below, the cited combination of references does not suggest all of the elements of the claimed invention, nor does the cited combination of references provide a motivation to combine the elements to create the claimed invention.

In particular, none of the cited references teach or suggest methods of detecting a precipitate formed within a few micrometers of the bound target compound on an array comprising a density of at least 20 discrete regions per cm^2 as recited in amended Claim 1, nor do they teach or suggest devices comprising such arrays comprising such precipitates as recited in amended Claim 14. Applicants note that support for the amendment to Claim 1 reciting that the precipitate is formed within a few micrometers of the bound target compound may be found in throughout the specification, including at page 6, lines 3-4 and page 9, lines 11-12. Applicants note that support for the amendment to Claim 14 reciting that apparatus comprises the solid support comprising an array may be found throughout the specification, including at page 10, lines 28-31, page 12, lines 2-14, page 14, lines 5-16, and Figures 2-7.

The Abouzied et al. reference discloses a colorimetric method of screening and detecting analytes on nitrocellulose (NC) membrane strips. In the method described in Abouzied, a colored reaction product formed through the action of an enzyme linked to the target analyte is used to detect the presence of the analyte in the sample. The method of detection includes

visually comparing color intensities formed by precipitates on the NC membrane and quantitatively assaying line density using a CCD camera. In the method disclosed in Abouzied, the lines on the NC membrane strips were spaced 0.25 cm apart (page 496, column 2).

As indicated in the specification at page 2, line 32 through page 3, line 11, colorimetric assays in which an enzyme generates a colored reaction product which forms a precipitate, such as the methods described in Abouzied, are unsuitable for use in arrays comprising a density of at least 20 discrete regions per cm^2 because the precipitate occupies an area which is too large to allow it to be localized to a single discrete region. In contrast, in the present invention, the precipitate forms within a distance of a few micrometers from the bound target molecule, thereby allowing it to be localized to a single position on an array comprising at least 20 discrete regions per cm^2.

With respect to the apparatus of Claim 14, Applicants note that Abouzied et al discloses a nitrocellulose strip being visualized by a camera which is connected to a computer to detect and/or quantify. However, the nitrocellulose strip of Abouzied, as previously discussed, is not a solid support comprising an array of at least 20 discrete regions per cm^2 and a precipitate positioned within a few micrometers of a bound target compound as recited in amended Claim 14.

Thus, there is no disclosure or suggestion in Abouzied of arrays comprising at least 20 discrete regions per cm^2 nor does this reference disclose or suggest formation of a precipitate within a few micrometers of a target compound bound to such arrays or devices comprising such arrays and such precipitates.

Like Abouzied, Roth discloses a method for localizing and quantitating a molecule in a sample. In the method of Roth, an enzyme generates a colored reaction product which precipitates. However, as discussed above, the precipitate generated through enzymatic reactions is too diffuse to be used with an array having a density of at least 20 discrete regions per cm^2 as in the present invention.

Furthermore, although Roth discloses the use of antibodies having gold particles fixed thereto along with silver intensification in the context of localizing a molecule in a cell or tissue, there is no disclosure or suggestion of using such techniques to detect the presence of a precipitate formed within a few micrometers of a target compound on an array having a density

of at least 20 discrete regions per cm^2 as in the present invention. Furthermore Roth teaches that methods using gold particles and silver intensification are undesirable or labor intensive in quantitative analyses (see Column 1, line 24-30). Thus, there is no disclosure or suggestion in Roth of arrays comprising at least 20 discrete regions per cm^2 nor does this reference disclose or suggest formation of a precipitate within a few micrometers of a target compound bound to such arrays or devices comprising such arrays and such precipitates.

Although Brown discloses a microarray having at least 10 distinct polynucleotides or polypeptides within an area of 1 cm^2 there is no disclosure or suggestion of detecting a precipitate formed within a few micrometers of a target compound bound to such arrays or devices comprising such arrays and such precipitates.

Howard III discloses a video test strip reader for detecting the presence of molecules bound to a test strip. The device of Howard is not used to detect a precipitate formed on a high density array as in the present invention but rather to read a signal from a test strip. There is no disclosure or suggestion of detecting the presence of a precipitate formed within a few micrometers of a target compound on an array having a density of at least 20 discrete regions per cm^2 as in the present invention or devices comprising such arrays and such precipitates.

Furthermore, with respect to the apparatus of Claim 14, although Howard III et al discloses a CCD camera equipped with illumination sources and a computer system (page 5) which can evaluate such information as barcodes, the apparatus disclosed in Howard is used with a test strip rather than an array having a density of at least 20 discrete regions per cm^2 and having a precipitate formed within a few micrometers of a target compound.

Terstappen discloses the use of magnetic beads to collect cells. However, there is no disclosure or suggestion in Terstappen of detecting the presence of a precipitate formed within a few micrometers of a target compound on an array having a density of at least 20 discrete regions per cm^2 as in the present invention or devices comprising such arrays and such precipitates.

Because none of the cited references teach or suggest detection of a precipitate formed within a few micrometers of a target compound on an array having a density of at least 20 discrete regions per cm^2 or devices comprising such arrays and such precipitates the cited references do not render the claimed invention obvious.

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Filed : May 19, 2000

New Claims

New Claim 28 recites that the precipitate is formed on the surface of a particle associated with the target compound. Support for new Claim 28 is found in the specification on page 8, lines 23-26.

New Claims 29-32 recite features of the claimed apparatus which were recited in original Claim 14 as filed on May 19, 2000.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully asserts that the present application is fully in condition for allowance. If any issues remain that may be addressed by a phone conversation, the Examiner is invited to contact the undersigned at the phone number listed below.

The changes made to the specification, the Abstract and the claims by the current amendment, including insertions and **[deletions]**, are shown on an attached sheet entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this amendment. No new matter has been added herewith.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification

The paragraphs on page 17, beginning at line 18 and ending at line 27 have been amended as follows:

[Short]Brief description of the drawings

[The f]Figure 1 compares the detection of target molecules obtained on arrays composed of DNA capture nucleotide sequences covalently fixed on glass and used to detect 3 concentrations of biotinylated target DNA either in fluorescence or after silver concentration.

The figures 2 to 7 represent the **[spatail]**spatial arrangement of some elements in various embodiments of the apparatus for performing the detection and/or the quantification method according to the invention**[.]**:

Figure 2 represents an embodiment of the apparatus comprising a solid support 1 above several regularly spaced illuminant sources 2 on a circular support 4 and two cameras 3, 3' placed above the solid support.

Figure 3 represents an embodiment of the apparatus comprising a solid support 1, above several regularly spaced illuminant sources 2 on a circular support 4 and a single camera 3 placed above the solid support.

Figure 4 represents an embodiment of the apparatus comprising two regularly spaced illuminant sources 2, 2', each on a circular support 4, 4'. The first set of sources 2 is placed above the solid support 1 and the second set of sources 2' is placed below the solid support. Both sets of illuminant sources are symmetrical to the solid support and a camera 3 is placed above the first illuminant source set.

Figure 5 represents an embodiment of the apparatus comprising a solid support 1 above the illuminant sources 2 which may or may not be regularly spaced from each other on a circular support 4. The camera 3 is placed above the solid support.

Figure 6 represents the camera 3 above the first illuminant source 2 on a circular support 4 as described in Figure 4. Both the camera and the illuminant source are above the solid support 1.

Figure 7 represents an embodiment of the apparatus comprising several regularly spaced illuminant sources 2 on a circular support below the solid support 1. Above the solid support are three cameras 3, 3', 3" in a triangular arrangement.

In the Abstract

The paragraph on page 29, beginning at line 7 and ending at line 25, has been amended as follows:

The present invention is related to a method for the identification and/or the quantification of a target compound obtained from a sample, preferably a biological sample, comprising the steps of**[**:

-]putting into contact the target compound with a capture molecule in order to allow a specific binding between **[said]**the target compound with a capture molecule, **[said]**the capture molecule being fixed upon a surface of a solid support according to an array comprising a density of at least 20 discrete regions per cm^2, each of **[said]**the discrete regions being fixed with one species of capture molecules, **[**

-]performing a reaction leading to a precipitate formed at the location of **[said]**the binding, determining the possible presence of precipitate(s) in discrete region(s), and **[**

-]correlating the presence of the precipitate(s) at the discrete region(s) with the identification and/or a quantification of **[said]**the target compound.

In the Claims

Claims 1, 14, 22 and 23 have been amended as follows:

1. **(Twice amended)** A method for the identification and/or the quantification of a target compound obtained from a sample, comprising the steps of:

putting into contact the target compound with a capture molecule in order to allow a specific binding between said target compound with a capture molecule, said capture molecule being fixed upon a surface of a solid support according to an array comprising a density of at least 20 discrete regions per cm^2, each of said discrete regions being fixed with one species of capture molecules,

performing a reaction leading to formation of a precipitate within a few micrometers of the bound target compound**[formed at the location of said binding]**,

determining the possible presence of precipitate(s) in said discrete region(s), and correlating the presence of the precipitate(s) at said discrete region(s) with the identification and/or a quantification of said target compound.

14. **(Twice amended)** A diagnostic and/or quantification apparatus **[of one or more identical or different target compound(s) obtained from a sample, which comprises]**comprising:

a solid support comprising an array comprising at least 20 discrete regions per cm^2, each of said regions being fixed with one species of a capture molecule which recognizes a target compound, target compounds bound to some of said capture molecules, and a precipitate present within a few micrometers of said bound target compounds;

a detection and/or quantification device **[of precipitate(s) formed at the location of a binding of said target compound with a capture molecule upon a surface of a solid support according to an array comprising at least 20 discrete regions per cm^2, each of said discrete regions being fixed with one species of capture molecule]**for detecting said precipitate; and

[possibly a reading device of information(s) recorded upon said solid support, and]

a computer programmed to **[possibly recognize discrete regions bearing capture molecules,]**collect the results obtained from said detection **[device, and possibly the information(s) obtained from said reading device, and carry out a diagnostic and/or quantification of said target compound(s)]**and/or quantification device.

22. **(Twice amended)** The apparatus according to Claim 15, which comprises, placed above the solid support, one camera and a first illuminant source and, under said camera, a second illuminant source placed under the solid support, the two illuminant sources being positioned to allow detection of said precipitate(s)**[placed almost symmetrically according to the position of the solid support]**.

23. **(Twice amended)** A computer**[program]** comprising program code stored thereon**[means]** for performing the steps of determining the possible presence of a precipitate in discrete regions and correlating the presence of said precipitate at the discrete regions with the identification and/or the quantification of a target compound, according to the method of Claim 1, when said program code is run on said**[a]** computer.